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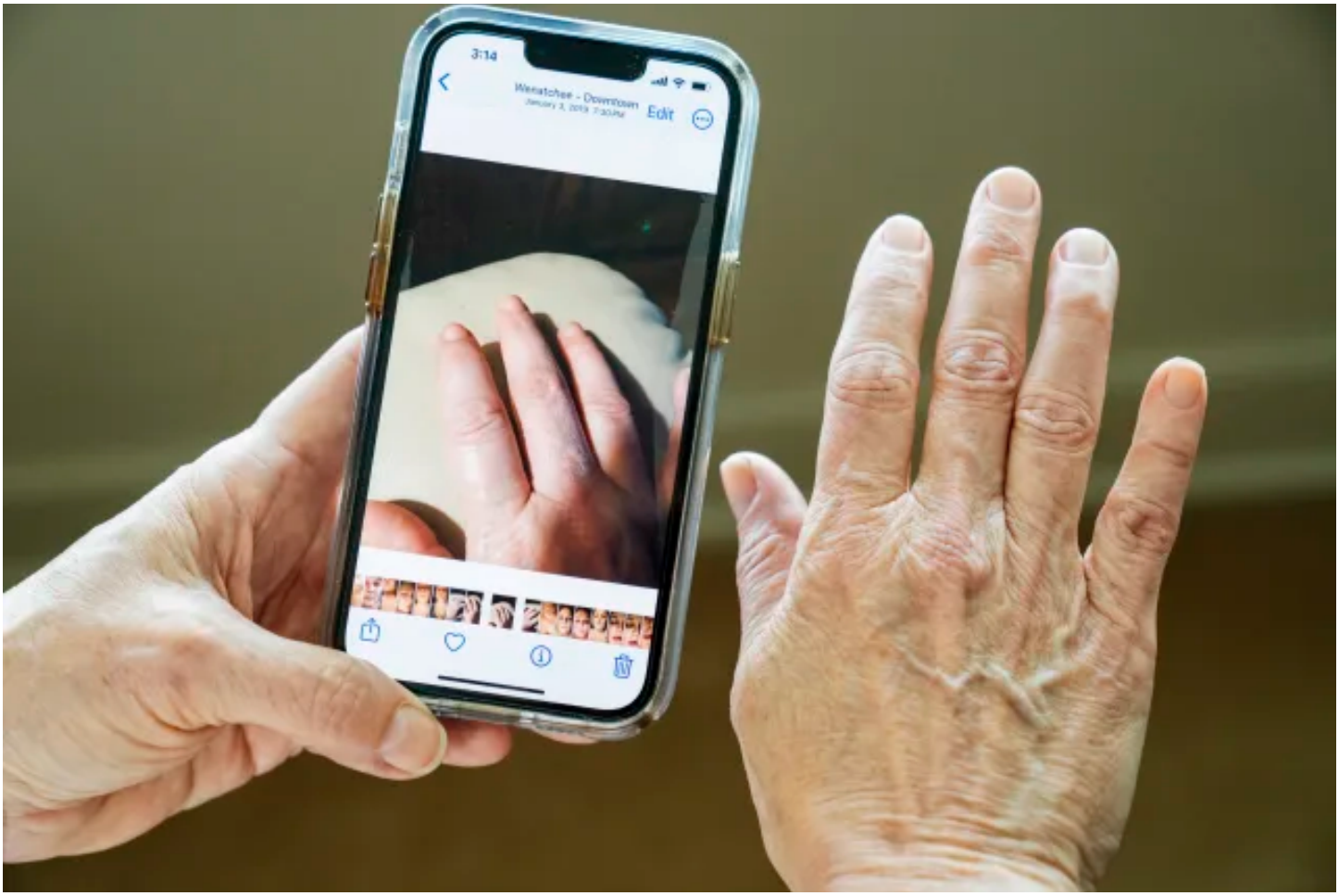
The New York Times

Doctors Test Obesity Drugs' Limits

Gina Kolata
Tue, June 18, 2024 at 7:43 a.m. EDT
8 min read



Lesa Walton compares her hand now to a photo when she experienced swelling and rheumatoid arthritis in 2019, at home in Wenatchee, Wash., June 3, 2024. (M. Scott Brauer/The New York Times) ... More

Lesa Walton suffered for years with rheumatoid arthritis. "It was awful," said Walton, 57, who lives in Wenatchee, Washington. "I kept getting sicker and sicker."

She also had high blood pressure, and she was obese. Doctors told her to diet and exercise,

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Then she found a doctor who prescribed Wegovy, one of the new obesity drugs. Not only did she lose more than 50 pounds, she said; her arthritis also cleared, and she no longer needed pills to lower her blood pressure. Her new doctor, Dr. Stefie Deeds, an internist and obesity medicine specialist in private practice in Seattle, said Walton exemplified a growing movement in obesity medicine.

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Proponents call it “obesity first.” The idea is to treat obesity with medications approved for that use. As obesity comes under control, they note, the patient’s other chronic diseases tend to improve or go away.

“We are treating the medical condition of obesity and its related complications at the same time,” Deeds said.

Others are wary. People with obesity can be put off when a doctor mentions their weight. And, yes, the new obesity drugs may have unexpected benefits beyond obesity, such as reducing inflammation. But the drugs are expensive, and many of the other potential gains have not been demonstrated in rigorous studies.

Dr. Gordon Guyatt, a clinical trials expert at McMaster University in Ontario, said the prudent approach is to use drugs — often inexpensive generics — that have been well tested and shown to treat conditions that often accompany obesity, such as high blood pressure, high

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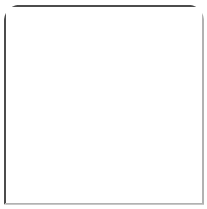

Itâ€™s Time to Change the Board Game

Yet, many physicians, like Deeds, are struck by stories like Walton's, which they say they often see in their practices. There is reason to believe that the drugs' effects on medical problems other than obesity may be independent of weight loss, they contend.

The idea of treating obesity first is a change from customary medical practice. When patients come in with obesity and other related chronic conditions such as high blood pressure, elevated blood sugar levels and sleep apnea, many doctors prescribe drugs for each condition. They may also advise exercise and changes to diet — but often without any clear guidance and, as decades of studies repeatedly showed, without any real prospects that most people will lose weight.

By starting with a powerful new drug for obesity, such as Wegovy from Novo Nordisk or Zepbound from Eli Lilly, in addition to diet and exercise, doctors hope that while they treat obesity, using just one drug, the related conditions will improve.

As Dr. Caroline M. Apovian, an obesity medicine specialist at Brigham and Women's Hospital in Boston, puts it, "You get the weight loss, and you've treated the high blood pressure, the fatty liver, the diabetes, the high cholesterol, the high triglycerides."

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Apovian, who has advised companies that make the obesity drugs, says that patients are thrilled to be taking one drug instead of many and, of course, to be losing weight after years of fruitless attempts at dieting.

Experts also describe another advantage: Patients often keep taking the obesity drugs, while many who are taking drugs they need to be healthy, such as statins, abandon them.

Still, there are as yet few examples of rigorous studies to show that medical conditions accompanying obesity go away when it is treated. Large clinical trials that randomly assign patients to an obesity treatment or a placebo are needed to establish whether the medicine has the hoped for effect on multiple conditions.

It may not.

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Medical history is stuffed with examples of treatments that everyone thought would work until a clinical trial showed they didn't.

Experts widely expected menopause hormones to prevent heart disease, and Wyeth, the maker at the time of the wildly popular Prempro, even asked the Food and Drug Administration to put heart disease protection on the drug's label. But when the National Institutes of Health conducted a large and rigorous study, the Women's Health Initiative, the researchers had to end the clinical trial early for safety reasons: Women taking the drug had an increased risk of heart disease, blood clots, strokes and breast cancer.

Then there was the federal study asking if beta carotene, a widely used antioxidant supplement, could reduce the risk of cancer and heart disease. The supplement did not, and it slightly increased the lung cancer risk among smokers and those exposed to asbestos.

Two federal studies looked into whether a high-fiber diet reduced the risk of colon cancer. The researchers were astonished to find no such evidence.

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Yet there is reason to think that the new obesity drugs could be different. They seem to have effects on the brain and the body that go far beyond quelling urges to eat.

Those effects can occur almost immediately, said Dr. Susan Z. Yanovski, co-director of the Office of Obesity Research at the National Institute of Diabetes and Digestive and Kidney Diseases. She noted that when Novo Nordisk conducted a clinical trial of Wegovy in people with heart disease, cardiac complications diminished early in the course of treatment, before the patients lost much weight.

The company now reports that they also had improvements in their kidney functions, independent of weight loss. Participants taking Wegovy who lost very little weight had the same sort of improvements in kidney functions as those who lost a lot.

A recent study by Novo Nordisk testing Ozempic in people with diabetes and kidney disease found the same thing: Kidney function was better preserved in the group taking Ozempic, an effect that was independent of weight loss. Dr. Florian M.M. Baeres, the company's corporate vice president of global medical affairs, noted that the participants' starting weight also did not matter. The effect on the primary outcome was the same, he said, "whether you start from a BMI above 30 or under 30."

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A large part of the effect may be the drugs' ability to reduce inflammation, said Dr. Daniel Drucker, an obesity researcher at the Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital in Toronto. It occurs before weight loss.

Drucker, who was involved in the discovery of the new drugs and consults for the companies that make them, was stunned by the response from patients after media outlets mentioned a paper he co-wrote showing that the obesity drug tirzepatide, or Zepbound, can reduce inflammation. In mice.

Not just in mice, patients told him in emails. A woman who suffered from rheumatoid arthritis for years sent Drucker pictures of her hands before and almost immediately after starting Zepbound for obesity. In the before photo, her hands were puffy and painful, despite the arthritis drugs she was taking. In the after photo, the swelling and pain were gone.

"Within a few days, all my joint pain went away," the woman said in a telephone interview; she requested anonymity out of concern that future employers might become aware of her illness.

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Eli Lilly and Novo Nordisk, the makers of Zepbound and Wegovy, are testing variations of the drugs in the hope that they will be even better in eliciting weight loss.

So far, in addition to the results in people with heart disease, Novo Nordisk found in another clinical trial that Wegovy improved physical functioning — such as an ability to exercise — in people with diabetes and heart failure. Eli Lilly found that Zepbound can help with sleep apnea. Other trials now underway are testing obesity drugs as treatments for depression, addiction, schizophrenia, Parkinson's disease and Alzheimer's disease. Dozens of other companies are working on new obesity drugs that may be applied to other conditions.

"This is the way clinical research on new drugs ought to be done," said Dr. Ezekiel Emanuel, co-director of the Healthcare Transformation Institute at the University of Pennsylvania.

But assessing which drugs effectively treat which conditions will take a long time. Clinical trials take years and cost millions of dollars. Many doctors may be unwilling to wait.

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“I’m very sympathetic to clinicians who say, ‘While the researchers are getting more data, we are going to try this approach,’” Emanuel said. It is common in oncology, he added, that once a drug is approved, doctors can use it for other illnesses, at their discretion.

With the obesity drugs, he added, the off-label experimenting — like a recent small study indicating that one of the drugs might slow the progression of Parkinson’s disease — shows “what a miraculous set of drugs these are,” with effects that were “totally unexpected.”

Others caution against “obesity first,” including representatives of companies like Eli Lilly and Novo Nordisk, saying that it is prudent to wait for results from clinical trials.

Dr. Scott Hagan, a Seattle primary care doctor, goes further, edging toward an “obesity last” approach. If a patient comes in with obesity and obesity-related conditions, he starts by treating the related conditions with drugs he knows can work. Only later, when the patients are comfortable with him, and if the other conditions are not improved, will he discuss trying the obesity drugs, Hagan said.

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People with obesity, he added, tend to have a long history of fraught relationships with doctors who blame them for their weight, despite their having spent years, even decades, trying diets and exercise. Many of them, he says, will be put off if the first thing he tries to treat is their obesity.

“My priority,” he said, “is establishing trust in a relationship.”

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THE HILL

Weight loss drug could help treat sleep apnea: Study

Lauren Irwin
Fri, June 21, 2024 at 6:00 p.m. EDT
1 min read

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A popular weight loss drug may be able to assist in the treatment of sleep apnea, a new study found.

Tirzepatide, the medicine found in the drug Zepbound and the obesity drug Mounjaro, reduced the severity of sleep apnea, a disorder that causes breathing to be interrupted, among other measures in patients who had obesity and took the medication for a year.

The study, published Friday in the New England Journal of Medicine, was conducted in two controlled trials involving adults with moderate to severe obstructive sleep apnea and obesity. The study found that tirzepatide reduced the apnea-hypopnea index, body weight, blood pressure and improved sleep, among other things.

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Patients who took the drug had their number of sleep apnea episodes reduced by about half to nearly 60 percent compared to just 10 percent who received a placebo.

Those who received the drug also lost about 18 percent to 20 percent of their body weight and showed other improvements, per the study.

Eli Lilly and Co. is the drug's maker and paid for the research, The Associated Press reported.

The company has asked the Food and Drug Administration to expand the use of the drug to be able to treat moderate to severe sleep apnea and a decision could come by the end of the year. An outside expert warned that more research will be necessary if it could be a sole treatment for sleep apnea, per the AP.

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The news wire also noted an estimated 20 million Americans are affected by sleep apnea, and the disorder can cause short-term issues like snoring, brain fog and daytime sleepiness and long-term issues like heart disease, dementia and death.

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Up next

THE CANADIAN PRESS

Obesity drug used in Mounjaro and Zepbound may help treat dangerous sleep apnea

Jonel Aleccia
Fri, June 21, 2024 at 6:22 p.m. EDT
3 min read

yahoo!news

A popular obesity drug may help treat a dangerous disorder in which people struggle to breathe while they sleep, a new study finds.

Tirzepatide, the medication in the weight-loss drug Zepbound and also the diabetes treatment Mounjaro, appeared to reduce the severity of sleep apnea along with reducing weight and improving blood pressure and other health measures in patients with obesity who took the drug for a year.

Eli Lilly and Co., the drug's maker who paid for the research, has asked the Food and Drug Administration to expand use of the drug to treat moderate to severe sleep apnea, in which people stop and start breathing during sleep, a spokesperson said Friday. A decision is expected by the end of the year.

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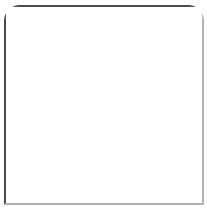
But an outside expert cautioned in an editorial that more research will be needed to tell if the drug can be used as “a sole treatment” for obstructive sleep apnea, which occurs when tissue in the throat relaxes and collapses during sleep, fully or partially blocking the airway. It affects an estimated 20 million Americans and can cause short-term issues such as snoring, brain fog and daytime sleepiness but also severe long-term issues such as heart disease, dementia and early death.

The research, published Friday in the New England Journal of Medicine and presented at a medical meeting, included nearly 500 people diagnosed with obesity and sleep apnea. Half of them used what's typically known as a CPAP machine that feeds oxygen through a mask to keep airways open during sleep. The other group included people for whom a CPAP machine had failed or wasn't tolerated.

The study found that patients in both groups who got weekly injections of tirzepatide reduced the number of episodes per hour in which their breathing slowed or stopped completely during sleep by about half to nearly 60%, compared to about 10% in people who got a dummy drug. Up to half of the patients taking tirzepatide reduced the apnea episodes enough to potentially resolve the disorder, compared with up to 16% of those using the placebo medication, according to the research.

On average, patients who took tirzepatide also lost between 18% and 20% of their body weight and showed improvements in blood pressure and a condition in which blood oxygen drops during sleep. Patients also reported better sleep and fewer sleep disturbances, the study found.



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The new research shows that tirzepatide is “a more effective knife in the drawer,” for treating sleep apnea, said lead author Dr. Atul Malhotra, a sleep medicine specialist at the University of California, San Diego.

In an accompanying editorial, Dr. Sanjay Patel, a sleep medicine specialist at the University of Pittsburgh, cautioned that whether tirzepatide can treat sleep apnea in real-world patients “remains unclear” because of the way improvement is measured. He also noted that cost and access remain obstacles to using tirzepatide and that the addition of the drug as a treatment could exacerbate racial and other disparities in addressing sleep apnea.

Dr. Paul Peppard, a sleep medicine researcher at the University of Wisconsin who was not involved in the study, said losing weight has long been recommended as a way to reduce the severity of sleep apnea by expanding lung capacity, reducing fat in the airways and improving oxygen usage. While diet and exercise can spur weight loss and reduce the consequences of the disorder, the ongoing obesity epidemic in the U.S. proves that shedding pounds is difficult for many people, he said. In such cases, medications such as tirzepatide can help.

“I expect that these drugs could be used as a tool to treat many of the established outcomes of obesity,” Peppard said.

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Jonel Aleccia, The Associated Press

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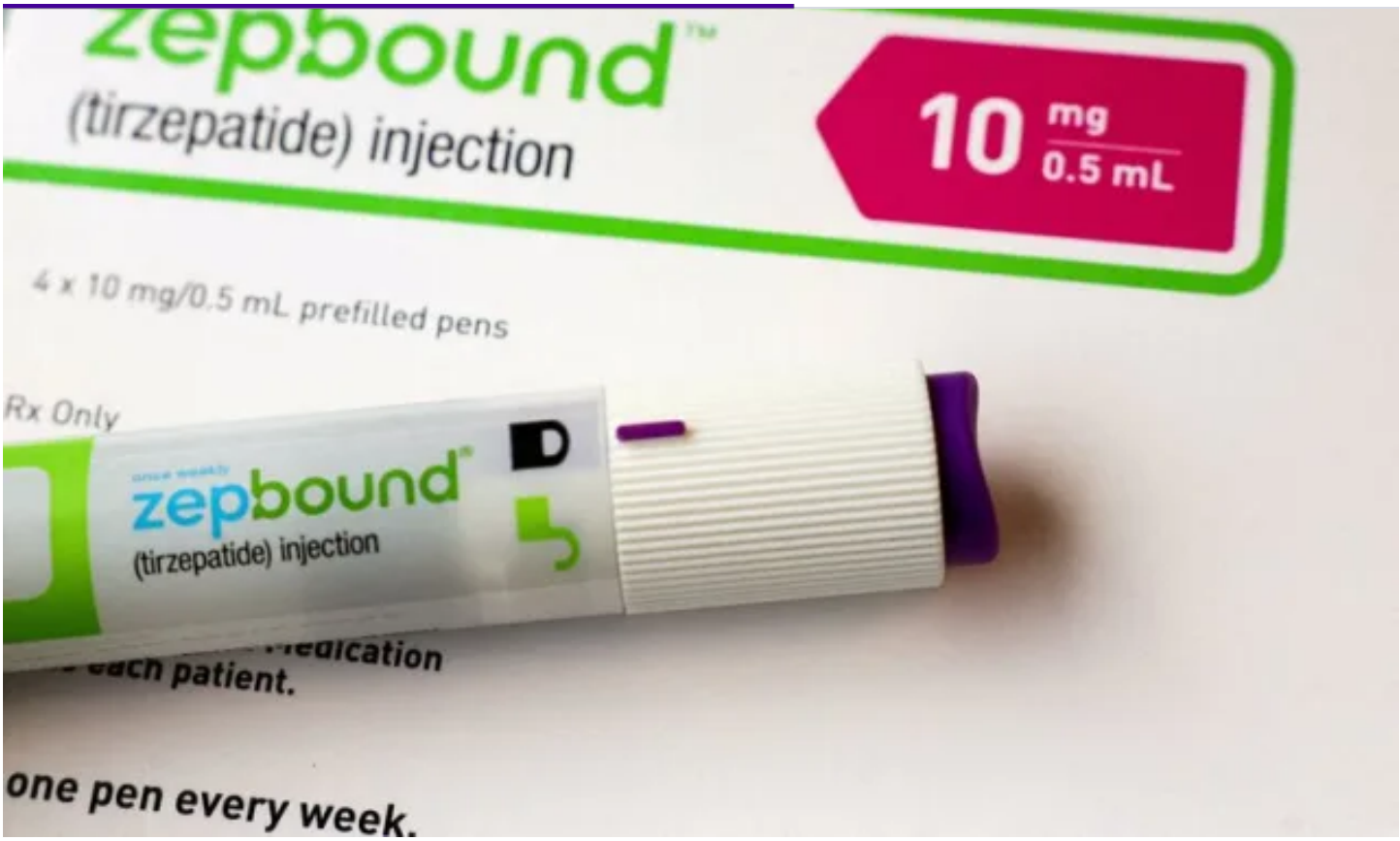
Up next

REUTERS

Weight-loss drug Zepbound resolves sleep apnea in up to 52% of patients, Lilly says

Patrick Wingrove
Updated Fri, June 21, 2024 at 5:10 p.m. EDT
2 min read

yahoo!news



FILE PHOTO: An injection pen of Zepbound, Eli Lilly's weight loss drug, is displayed in New York

By Patrick Wingrove

(Reuters) - Eli Lilly on Friday said its popular weight-loss drug Zepbound helped resolve moderate to severe obstructive sleep apnea in up to 52% of patients in two late-stage trials.

U.S.-based Lilly and Danish rival Novo Nordisk are in a race to get their obesity drugs approved to treat other ailments. Novo's Wegovy was approved as a treatment for heart disease in March, while Lilly's own heart-disease trial for Zepbound is expected to conclude this year.

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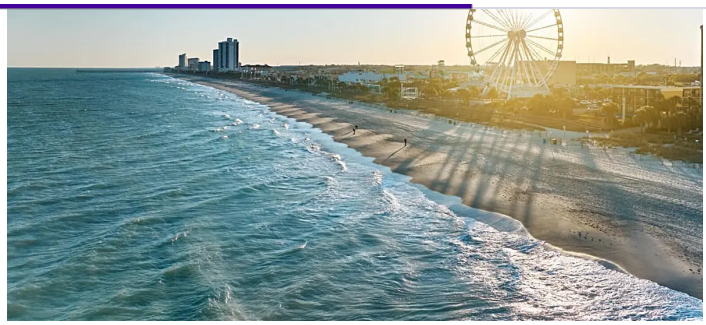

The Beach for Everyone

Lilly in April said Zepbound, known chemically as tirzepatide, helped reduce episodes of irregular breathing in patients with obstructive sleep apnea by 55% in the first study and by 62.8% in the second.

Patients in the first study received tirzepatide, while patients in the second tested the drug in combination with continuous positive airway pressure (PAP) therapy, in which air is pumped into the lungs to keep the airway open during sleep.

Full results from the trials, presented Friday at the American Diabetes Association's scientific meeting in Orlando, Florida, showed Zepbound helped resolve sleep apnea in 43% of patients taking the drug alone and in 51.5% of those also using PAP.

The criteria for disease resolution was patients experiencing fewer than five episodes of shallow or no breathing per hour during sleep, or five to 14 episodes and not being excessively sleepy during the day, according to Lilly.

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Lilly said 14.9% of patients on a placebo also achieved disease resolution in the first study, along with 13.6% in the second.

Friday's data showed Zepbound helped lower biomarkers related to sleep apnea, including oxygen desaturation, blood pressure, and C-reactive proteins - signs of inflammation that can indicate heart disease - Lilly said.

The drugmaker said it had submitted its application to the U.S. Food and Drug Administration to have Zepbound approved as a treatment for obstructive sleep apnea and would submit to other regulatory agencies globally in the coming weeks.

Lilly said the overall safety of tirzepatide in these trials was similar to past studies, with the most frequent side effects being diarrhea, nausea, vomiting and constipation.

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The Indianapolis-based drugmaker presented data earlier this month showing Zepbound helped treat liver scarring in patients with a difficult-to-treat fatty liver disease called metabolic dysfunction-associated steatohepatitis, or MASH.

(This story has been corrected to change the percentage of patients on a placebo who achieved disease resolution in the second study from 6.4% to 13.6% in paragraph 7)

(Reporting by Patrick Wingrove; editing by Caroline Humer and Rod Nickel)

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Up next

HUFFPOST

The 1 Unexpected Sign Of Colon Cancer, According To Doctors

Jillian Wilson
Sun, June 23, 2024 at 3:00 a.m. EDT
4 min read

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While not the most common sign, narrow stools can be indicative of colorectal cancer. Tetra Images via Getty Images

With more and more young people being diagnosed with colorectal cancer, it's natural to be nervous about the disease.

Rates of colorectal cancer in people under 50 have been increasing since the 1990s, according to Dr. Michael Cecchini, a co-director of the colorectal program at the Center for Gastrointestinal Cancers and medical oncologist at Yale Cancer Center.

The exact reason why rates are increasing is unknown. Experts "think it's something lifestyle and environmental, but exactly what that is, we don't know," Cecchini said. Researchers are investigating what could be happening. In the meantime, it's important that you stay alert about colorectal cancer — even if you're young.

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Part of this is knowing the warning signs. And there's one surprising symptom in particular that's been gaining attention on social media: pencil-thin poop.

As one TikTok user explained on the platform, she noticed that her stools were thinner than normal, along with other red-flag symptoms like unexplained weight loss and diarrhea. She thought that she had irritable bowel syndrome, so she didn't go to the doctor at first. When she finally did, she was diagnosed with stage 4 colon cancer.

Here's what experts say about this particular issue:

Narrow stool can be a red flag.

Doctors will sometimes see patients whose "stools are much thinner, or they're pencil in thickness and size, which is a description that some patients with colorectal cancer will have," Cecchini said.

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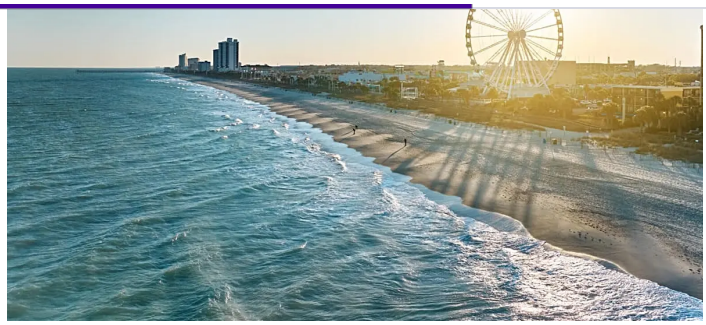

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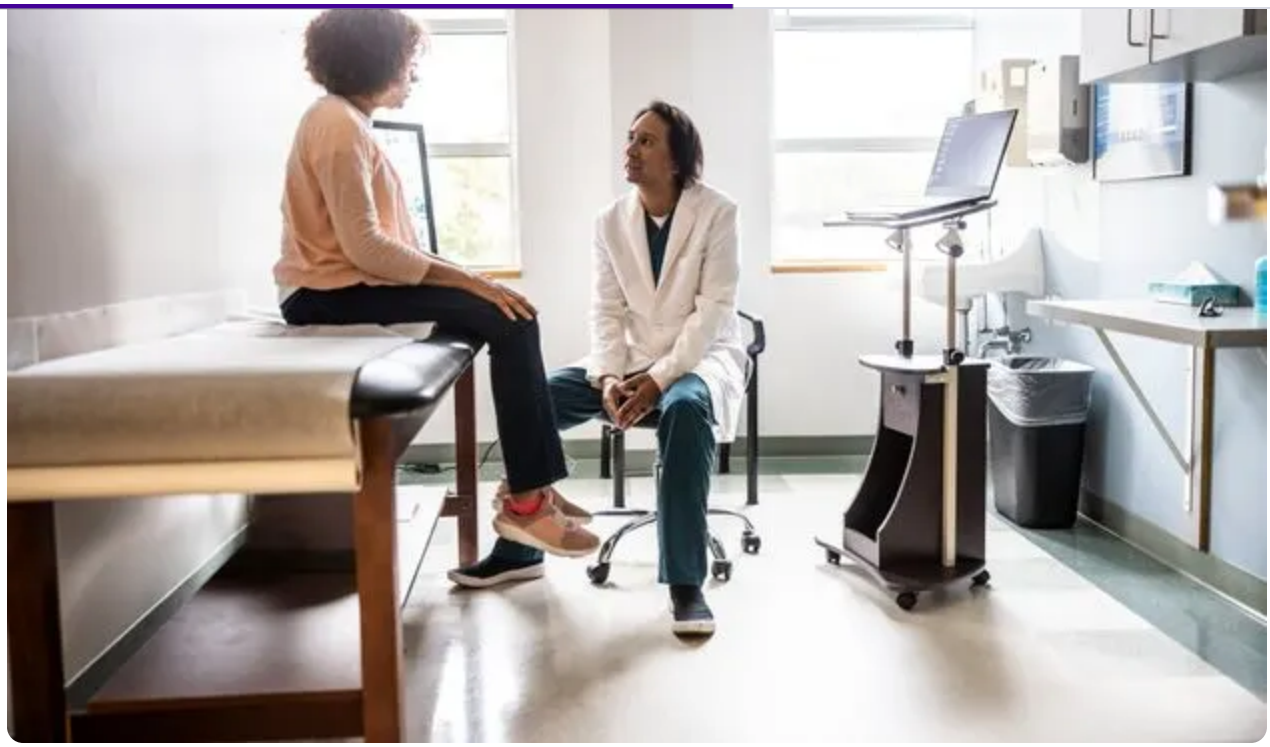
This tends to occur if tumors are present near the end of the colon or if they line the entire inside of the colon, which narrows whatever stool passes through, Cecchini explained.

Healthy stool should be long and sausage-shaped, according to Medical News Today, and come out as one piece or several smaller pieces. What's most concerning is when thin stools are a new change that's persistent, said Dr. Jeffrey Dueker, a gastroenterologist at UPMC and an associate professor of gastroenterology at the University of Pittsburgh School of Medicine.

According to Dueker, any noticeable alteration in your bowel habits could be a potential red flag (but, he stressed, is not *always* a sign of colon cancer). In addition to a change in stool shape or consistency, this can include going to the bathroom more or less often.

Pencil-thin poop is one of the less common signs of colorectal cancer. "When it exists, it is highly concerning," Cecchini said. "It's just not one of the more common symptoms of the disease." The more widespread signs are blood in the stool and abdominal pain. Unintentional weight loss is another sign. And some cases of colorectal cancer have no symptoms at all.



Flag any concerning symptoms to your physician. MoMo Productions via Getty Images

If you notice any symptoms, you should tell your doctor.

You should never discount your symptoms, Cecchini said, if you notice blood in your stool, chronic abdominal pain, a change in bowel movements, or unexplained weight loss, it's important that you tell your doctor.

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"It's very easy in younger individuals to think, 'Oh, it's just hemorrhoids,' or something like that ... and it may be, but also those things can coexist," said Cecchini. "People certainly have hemorrhoids and cancer, or it can be something else completely."

In general, getting a colonoscopy or another colorectal cancer screening is the best way to lower your risk or catch it in the early stages. You can undergo "screening with colonoscopy or stool-based tests," Cecchini said. Chat with your doctor to determine the best screening for you.

For most people, screenings start at 45. But if you have any of the symptoms mentioned above or meet certain criteria, you may be eligible for a colonoscopy before 45, Dueker said.

"Anyone with a first-degree relative — mother, father, brother, sister, son or daughter — that has had colon cancer, especially if that person was diagnosed before the age of 50, is going to be at higher risk for colorectal cancer because of that family history, and should speak to their doctor about when they should start getting colonoscopies," Dueker explained.

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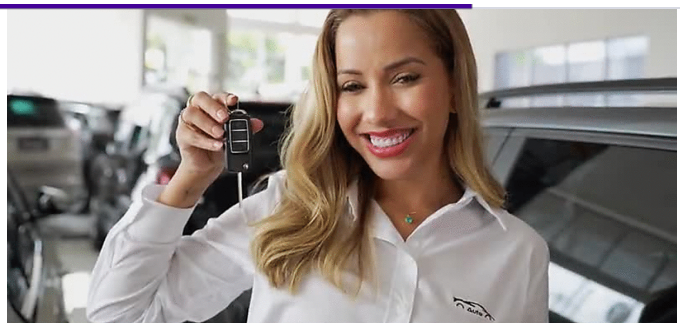

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If you've had inflammatory bowel disease or radiation treatment to the pelvic or abdominal area, or if you have certain genetic syndromes or a personal history of colon cancer, you would also want to get a colonoscopy before 45, Dueker noted.

Suffice to say, it's important to keep your doctor informed of your medical history and any potential issues you might be experiencing. But while you should take all of this seriously, you also shouldn't panic.

"All of these symptoms don't necessarily mean ... you have colon cancer," said Dueker. Instead, they could mean that a colonoscopy is necessary to determine what is going on. And while the cause *could* be colon cancer or a precancerous polyp, detecting the disease early is the best way to manage it.

"It's important to catch cancer early through screening or alerting to some of ... these symptoms so that we diagnose cancer at an earlier stage, where it's more treatable and hopefully curable," Cecchini said. "We still cure the majority of people with this cancer every year."

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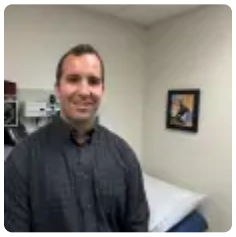

Guilty Eats

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